CLAIMS

1. An automated method for the large-scale *in vitro* screening of cells secreting at least one specific monoclonal antibody with affinity for a compound of interest, said method comprising at least the following steps:
(10) distribution of antibody-producing cells in at least one well of at least one culture plate;
(12) culturing said cells under conditions allowing their growth, with concomitant detection of cellular growth and of the quality of the cultures;
(14) iterative screening of said cells for the secretion of antibodies, with cloning of the cells secreting at least one antibody interacting with said compound of interest; and
(16) selection of at least one cell secreting one specific monoclonal antibody with affinity for said compound of interest.

2. The method as claimed in claim 1, characterized in that said compound of interest is an antigen comprising at least one epitope.

3. The method as claimed in claim 2, characterized in that said antigen is chosen from: proteins, nucleic acids, viral particles, synthetic peptides, chemical compounds, organs, organelles, whole cells, subcellular fragmentations.

4. The method as claimed in claim 3, characterized in that said antigen is a tumor cell.

5. The method as claimed in claim 1, characterized in that said distribution according to step (10) is carried out in an amount of at least 3×10^5 cells per well.

6. The method as claimed in claim 1, characterized in that each step is performed in a sterile atmosphere.

7. The method as claimed in claim 1, characterized in that said step (10) is at least preceded by the following preliminary steps:
(1) immunization of at least one animal, with said compound of interest;
(2) optionally, measurement of the immune response of said animal; and
(3) recovery of the antibody-producing cells.

8. The method as claimed in claim 1, characterized in that said step (10) is at least preceded by the following preliminary steps:
(0) bringing at least one dendritic cell and said compound of interest into contact, such that said dendritic cell presents at least one epitope of said compound of interest;
(1) immunization of at least one animal, with said dendritic cell presenting said epitope;
(2) optionally, measurement of the immune response of said animal; and
(3) recovery of the antibody-producing cells.

9. The method as claimed in claim 8, characterized in that when said compound of interest is a tumor cell, said step (0) comprises at least:
(01) the fusion of said dendritic cell and said tumor cell; and
(02) the recovery of at least one hybrid dendritic cell.

10. The method as claimed in claim 7 or 8, characterized in that said preliminary steps additionally comprise:
(4) the fusion of said antibody-producing cells with immortalized cells; and
(5) the recovery of the immortalized antibody-producing cells.

11. The method as claimed in claim 7 or 8, characterized in that said antibody-producing cells are chosen from mouse, rat, rabbit or human cells.

12. The method as claimed in claim 11, characterized in that said antibody-producing cells are mouse cells.

13. The method as claimed in any one of claims 7 to 12, characterized in that said preliminary steps are not automated.

14. The method as claimed in claim 1, characterized in that said iterative screening step (14) comprises at least the following screening module, which may be repeated:

- transfer of the culture medium collected from at least one well of at least one culture plate, into at least one well of at least one screening plate;
- screening of the cells for at least one given selection criterion;
- selective subculturing of the cells satisfying said criterion into at least one well of at least one new culture plate; and

- culture of said cells under conditions allowing their growth, with concomitant detection of cell growth and of the quality of the cultures.

15. The method as claimed in claim 14, characterized in that said step (14) comprises a prescreening module in which said selection criterion is the secretion of antibodies:
(140) transfer of the culture medium to at least one well of at least one screening plate;
(141) prescreening of the cells for the secretion of antibodies;
(142) selective subculturing of the cells secreting at least one antibody on at least one culture plate; and
(143) culture of said cells.

16. The method as claimed in claim 14, characterized in that said step (14) comprises a primary screening module in which said selection criterion is the secretion of antibodies interacting with said compound of interest:
(144) transfer of the culture medium to at least one well of at least one screening plate;
(145) primary screening of said cells for the secretion of at least one antibody interacting with said compound of interest;
(146) cloning of the cells secreting at least one antibody interacting with said compound of interest;
(147) subculturing of the cloned cells on at least one culture plate; and
(148) culture of said cells.

17. The method as claimed in claim 16, characterized in that said primary screening module is used after said prescreening module as claimed in claim 15.

18. The method as claimed in claim 16 or 17, characterized in that said step (14) additionally comprises a secondary screening module, in which said selection criterion is the secretion of monoclonal antibodies specific for said compound of interest:
(149) transfer of the culture medium to at least one well of at least one screening plate;
(150) secondary screening of said cells for the secretion of a monoclonal antibody specific for said compound of interest;
(151) selective subculturing of the cells secreting a monoclonal antibody specific for said compound of interest on at least one culture plate; and
(152) culture of said cells.

19. The method as claimed in claim 18, characterized

in that said step (14) additionally comprises a tertiary screening module, in which said selection criterion is the secretion of specific monoclonal antibodies with affinity for said compound of interest:
(153) transfer of the culture medium to at least one well of at least one screening plate;
(154) tertiary screening of said cells for the secretion of a specific monoclonal antibody with affinity for said compound of interest; and
(155) optionally, selective subculturing of the cells secreting a specific monoclonal antibody with affinity for said compound of interest on at least one culture plate; and
(156) optionally, culture of said cells.

20. The method as claimed in claim 1, characterized in that said step (16) comprises:
(16) the selection of at least one cell secreting a monoclonal antibody with specificity and/or affinity for said compound of interest greater than those of the monoclonal antibodies secreted by the other cells.

21. The method as claimed in claim 1 or 14, characterized in that said culture is carried out over a period of between at least 7 days and at most 21 days, said period being preferably between 7 and 15 days.

22. The method as claimed in claim 14, characterized in that a cell library is prepared for at least one screening module.

23. The method as claimed in claim 15, characterized in that said step (141) comprises at least:
(1411) the detection of the secretion of antibodies; and
(1412) the selection of cells secreting at least one antibody.

24. The method as claimed in claim 23, characterized in that said step (1411) comprises at least:
(14111) the collection of at least one culture supernatant sample; and
(14112) the detection of the secretion of antibodies in said sample.

25. The method as claimed in claim 23, characterized in that said step (1411) comprises at least the detection of the secretion of antibodies directly in the wells.

26. The method as claimed in claim 16, characterized

in that said step (145) comprises at least:
(1451) the collection of at least one culture supernatant sample;
(1452) the detection, in said sample, of the interaction of the antibodies with said compound of interest; and
(1453) the selection of cells secreting at least one antibody interacting with said compound of interest.

27. The method as claimed in claim 18, characterized in that said step (150) comprises at least:
(1501) the collection of at least one culture supernatant sample;
(1502) the detection, in said sample, of a specific interaction between a monoclonal antibody and said compound of interest; and
(1503) the selection of cells secreting a monoclonal antibody specific for said compound of interest.

28. The method as claimed in claim 19, characterized in that said step (154) comprises at least:
(1541) the collection of at least one culture supernatant sample; and
(1542) the measurement of the affinity of a monoclonal antibody for said compound of interest.

29. The method as claimed in claim 28, characterized in that step (1542) comprises at least:
(15421) the measurement of the affinity of a monoclonal antibody for said compound of interest; and
(15422) the identification and/or the location of at least one epitope of said compound of interest.

30. The method as claimed in claim 29, characterized in that said steps (15421) and (15422) are concomitant.

31. The method as claimed in claim 28, characterized in that step (154) additionally comprises:
(1543) the classification of the monoclonal antibodies on the basis of their specificity and/or their affinity for said compound of interest.